BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61B 19/00 — A1

(11) International Publication Number: WO 99/30629

(43) International Publication Date: 24 June 1999 (24.06.99)

(21) International Application Number: PCT/US98/26825

(22) International Filing Date: 17 December 1998 (17.12.98)

(30) Priority Data:
08/991,823 17 December 1997 (17.12.97) US
09/078,944 14 May 1998 (14.05.98) US

(71) Applicant: HEMODYNAMICS, INC. [US/US]; P.O. Box 4741, San Clemente, CA 92674 (US).

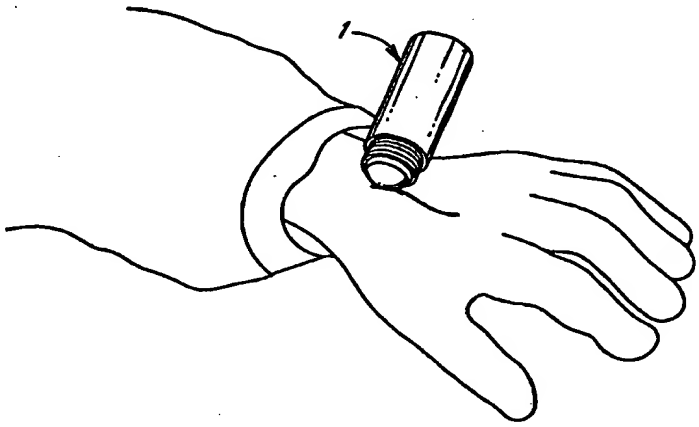
(72) Inventor: HAMMERSLAG, Julius, G.; 27011 Calle Esperanza, San Juan Capistrano, CA 92675 (US).

(74) Agent: ALTMAN, Daniel, E.; Knobbe, Martens, Olson & Bear, 16th floor, 620 Newport Center Drive, Newport Beach, CA 92660-8016 (US).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: SEALING MEDIA FOR SURGERY AND WOUND CLOSURE



(57) Abstract

A medical grade sealing media is used to seal a surface to a tissue of a mammal. The sealing media includes an adhesive with dispersed microparticulate material, and can be incorporated into a wound closure device.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	**ES**	Spain	**LS**	Lesotho	**SI**	Slovenia
AM	Armenia	**FI**	Finland	**LT**	Lithuania	**SK**	Slovakia
AT	Austria	**FR**	France	**LU**	Luxembourg	**SN**	Senegal
AU	Australia	**GA**	Gabon	**LV**	Latvia	**SZ**	Swaziland
AZ	Azerbaijan	**GB**	United Kingdom	**MC**	Monaco	**TD**	Chad
BA	Bosnia and Herzegovina	**GE**	Georgia	**MD**	Republic of Moldova	**TG**	Togo
BB	Barbados	**GH**	Ghana	**MG**	Madagascar	**TJ**	Tajikistan
BE	Belgium	**GN**	Guinea	**MK**	The former Yugoslav Republic of Macedonia	**TM**	Turkmenistan
BF	Burkina Faso	**GR**	Greece			**TR**	Turkey
BG	Bulgaria	**HU**	Hungary	**ML**	Mali	**TT**	Trinidad and Tobago
BJ	Benin	**IE**	Ireland	**MN**	Mongolia	**UA**	Ukraine
BR	Brazil	**IL**	Israel	**MR**	Mauritania	**UG**	Uganda
BY	Belarus	**IS**	Iceland	**MW**	Malawi	**US**	United States of America
CA	Canada	**IT**	Italy	**MX**	Mexico	**UZ**	Uzbekistan
CF	Central African Republic	**JP**	Japan	**NE**	Niger	**VN**	Viet Nam
CG	Congo	**KE**	Kenya	**NL**	Netherlands	**YU**	Yugoslavia
CH	Switzerland	**KG**	Kyrgyzstan	**NO**	Norway	**ZW**	Zimbabwe
CI	Côte d'Ivoire	**KP**	Democratic People's Republic of Korea	**NZ**	New Zealand		
CM	Cameroon			**PL**	Poland		
CN	China	**KR**	Republic of Korea	**PT**	Portugal		
CU	Cuba	**KZ**	Kazakstan	**RO**	Romania		
CZ	Czech Republic	**LC**	Saint Lucia	**RU**	Russian Federation		
DE	Germany	**LI**	Liechtenstein	**SD**	Sudan		
DK	Denmark	**LK**	Sri Lanka	**SE**	Sweden		
EE	Estonia	**LR**	Liberia	**SG**	Singapore		

SEALING MEDIA FOR SURGERY AND WOUND CLOSURE

Background of the Invention

The present invention relates to medical grade sealing media or used for wound closure and surgical procedures. More particularly, the present invention relates to surgical sealing media of the type useful for preventing or minimizing leakage through a joint formed between native tissue and adjacent native tissue or between native tissue and non-native tissue or material such as a heart valve, graft, or other prosthetic implant. Additionally, more particularly the present invention relates to sealing media of the type useful for bonding adjacent sections of skin separated by percutaneous incision or traumatic injury.

Sealing media for surgery:

Surgical heart valve replacement, for example, may involve implantation of one of three distinct prosthesis types: mechanical (synthetic), bioprosthetic (chemically-fixed porcine valve or bovine pericardium), or human allograft. These prostheses can provide effective hemodynamic improvement for replacement of native aortic, mitral or other valves that are either congenitally malformed or have been damaged by degenerative changes or disease resulting in either perfusion insufficiency or stenosis. Of the approximately 55,000 aortic valve implants annually in the U.S., 75% are mechanical valves. The remainder of the replacements are of transplanted tissues. Of these, over 80% are porcine bioprostheses; the relatively small number of allografts (2,500 per year) is primarily due to their limited availability.

The criteria for an ideal prosthesis would include natural hemodynamics, long-term durability, low incidence of thromboembolic complications, freedom from calcification, proven lack of immunogenicity and no inappropriate hyperplastic responses following implantation. In addition, the elimination of leakage around the sutured joint while retaining low thromboembolic and other complications of the prosthesis as implanted would be desirable.

When it is necessary to repair or replace a malfunctioning heart valve within a patient, the repair or replacement has traditionally been accomplished by a major open-heart surgical procedure, requiring general anesthesia and full cardiopulmonary by-pass with complete cessation of cardiopulmonary activity. The use of extracorporeal cardiopulmonary by-pass for cardiac support has become well established and has involved median sternotomy or less commonly thoracotomy. Such surgery usually includes one to two weeks of hospitalization and months of recuperation time for the patient. The average mortality rate with this type of procedure is about five to six percent, and the complication rate is substantially higher. Descriptions of open-heart procedures for replacing heart valves can be found in Gibbon's Surgery of the Chest., 5th Ed., David C . Sabiston, Jr., M.D., Frank D. Spencer, M.D., 1990, Vol. II Ch. 52, pp. 1566-1596, and Textbook of Interventional Cardiology, Eric J. Topol, 1990, Chs. 43-44, pp. 831-867.

Endovascular surgical procedures on the heart have been developed recently which, in contrast to open-heart surgical procedures, may have a reduced mortality rate, may require only local anesthesia, and may

necessitate only a few days of hospitalization. Minimally invasive procedures both on an arrested heart and, more recently, on a beating heart are also in development.

Notwithstanding the foregoing significant advances, the success of many procedures still depends upon the provision of a leak-proof joint between two sutured materials. Regardless of the entry pathway, for example, a replacement heart valve must be sutured to the annulus of the patient's heart. Coronary artery bypass grafts, peripheral vascular grafts, and any of a wide variety of organ transplants, among other procedures, include a risk of leakage through the sutured joint. In many procedures, particularly arterial side procedures such as a heart valve replacement, one portion of the procedure is dedicated to testing the sutured joint under arterial pressure and examining for leaks. Leakage often occurs to some degree, and clinical judgment exercised on the spot governs whether additional steps should be taken to minimize the leak or whether it will likely resolve itself before adverse consequences occur.

Thus, there remains a need for a simple and effective method and composition for minimizing high pressure leaks at a sutured joint. Preferably, the method and composition can be utilized with minimal training time and risk of error, and will not materially increase thromboembolic complications, immunogenicity, inappropriate hyperplastic responses, or other negative factors.

Sealing media for wound closure:

Every year, over 10 million traumatic wounds are treated by emergency physicians in the United States. A great many incisions ranging from a few millimeters to several centimeters in length are closed each year by medical personnel. Countless more less serious wounds are treated by non-medical persons, such as athletic trainers, parents of an injured child, or the injured individual himself.

Small wounds and lacerations may be treated by simply bandaging the wound or by using tape to keep the edges of the wound in apposition. Such methods may be performed with a minimum of time and training, as well as causing little or no additional trauma to the wound or causing the patient additional pain.

More serious wounds or incisions are generally treated by conventional methods such as suturing. Suturing requires the use of a needle and often involves a local anesthetic. Suturing can be costly because it is time-intensive and the procedure requires that the individual performing it have some medical training. Additionally, suturing can be painful and the use of needles may cause further distress for an already traumatized patient, as well as expose medical personnel to potential needlestick injury. Furthermore, because most sutures used topically do not dissolve, the patient generally must make a return visit at a later date for the often uncomfortable procedure of removal of the sutures.

In recent years, some medical personnel have tried using cyanoacrylate tissue adhesives as an alternative for such conventional methods. The most commonly used cyanoacrylates, which include ethyl- and butylcyanoacrylate, have some advantages over suturing, such as faster and less painful closure. They do,

however, have several drawbacks, most notably that they have a very low viscosity making precise application difficult, form a closure which is hard, brittle, and inflexible, and set up too quickly and do not allow for adjustment of the opposing skin surfaces.

Thus, there remains a need for a simple and effective method and composition for effecting wound closure. Preferably, the method and composition can be utilized with minimal training time and risk of error, and will not materially increase complications, immunogenicity, scarring, infection, or other negative factors.

Summary of the Invention

There is provided in accordance with one aspect of the present invention a medical grade sealing media for securing and sealing a surface to a tissue of a mammal. The medical grade sealing media comprises an adhesive and a microparticulate material. In one embodiment, the adhesive comprises cyanoacrylate. In another embodiment the microparticulate matter comprises silica.

In accordance with another aspect of the present invention, the medical grade sealing media is used for securing and sealing a surface to a tissue of a mammal. The Use comprises bringing a first surface and a second surface together in an adjacent configuration to form a joint, and thereafter securing the first surface to the second surface with a primary securing structure. The medical grade sealing media comprising an adhesive component and a micro-particulate component is delivered to one or more interfaces of the first surface and the second surface in a quantity sufficient to seal the joint between the first surface and the second surface.

In accordance with another aspect of the present invention, there is provided a wound closure device. The device comprises a reservoir containing wound closure media, said media comprising an adhesive compound and a microparticulate component, and an applicator tip. In one embodiment, the reservoir is compressible or collapsible. Optionally, the applicator tip comprises a roller ball. In another aspect the device is sterilized and disposable.

In accordance with another aspect of the present invention, there is provided a wound closure dressing. The dressing comprises a flexible support structure impregnated with wound closure media. The wound closure media comprises an adhesive component and a microparticulate component. In one embodiment the dressing further comprises a sealed pouch surrounding and containing the wound closure dressing.

Further features and advantages of the present invention will become apparent to those of skill in the art in view of the detailed description of preferred embodiments which follows, when considered together with the attached drawings and claims.

Brief Description of the Drawings

Figure 1 is a cross-section of a rollerball container-applicator as may be used to apply wound closure media in accordance with the present invention.

Figure 2 depicts the use of a rollerball container-applicator of the type in Figure 1 to deliver wound closure media to a topical wound to effect closure in accordance with the present invention.

Figure 3 is a view of an alternate container-applicator for use in accordance with the present invention.

Figure 4 is a cross-section of the container-applicator of Figure 3.

Figure 5 is a blown-up view of the applicator tip of the container-applicator of Figure 3 showing the placement of a break-away sealing tip.

Detailed Description of the Preferred Embodiments

Sealing media for surgery:

In accordance with the present invention, a sealing medium is used in conjunction with a primary wound closure or tissue fastening system in order to minimize or eliminate leakage at the interface of the surfaces being joined. The primary closure system may comprise sutures, staples, clamps, wires, or any other physical structure designed to retain two surfaces to be joined in contact with each other. The sealing media of the present invention may also be used alone, as a primary closure or fastening system.

The surfaces to be joined in accordance with the present invention may be two adjacent surfaces of native tissue which have been separated, such as by an incision. Alternatively, a first surface to be joined may be a surface of tissue in the patient, and the second surface to be joined may be an autologous tissue from elsewhere in the same patient such as a harvested vessel, allograph tissue such as a human transplant organ from a separate donor, animal tissue such as porcine or bovine heart valves, which may have been pretreated in accordance with known technology, or any of a wide variety of nontissue materials. Nontissue materials suitable for use with the present invention include any of a variety of biologically compatible metals such as stainless steel, gold, platinum, or others well known in the medical device industry. Alternatively, the second surface may be any of a wide variety of polymeric materials, including polyethylenes, polypropylenes, nylons, polytetrafluoroethylene and other polyfluoro compounds, polyesters such as Dacron, and other polymeric materials known in the art.

The second surface may also be a surface on any of a wide variety of implantable prostheses, prosthetic devices, grafts or organs. For example, the sealant of the present invention may be useful in heart transplant, kidney transplant, liver transplant, lung transplant or other transplant procedures. In addition, a wide variety of vascular grafting procedures can benefit from the use of the present invention, including tissue grafts using vessels harvested from elsewhere in the patient's body, as well as prosthetic grafts of the type which may be made from PTFE, Dacron, or other materials alone or in combination with supporting metallic cages. In addition, the present invention has particular application in connection with the implantation of replacement heart valves which will be subject to arterial pressure. Such valves may include mechanical valves, bioprosthetic valves, and human allografts.

Although specific prostheses, prosthetic devices, grafts and organs are named and discussed in this specification, such use of the terms should not be construed as limiting the definitions of these terms. It is the applicant's intention that these terms be given their broad ordinary meanings. Additionally, the terms device, graft, prosthesis and organ should be interpreted as including any skirts, supports, coverings or additional materials attached to or associated with the device, graft, prosthesis or organ.

The present invention may be used to relieve both acute and long-term risks of leakage at a joint. Acute risks may arise from such things as improper tensioning of the suture, the placement of the sutures around the annulus (in the case of a heart valve replacement), and complications resulting from diseased or damaged tissue. Diseased or damaged tissue, such as calcification in a blood vessel, may also give rise to long-term leakage risks, in that such conditions can present an opportunity for sutures to work loose over time. The tissue adhesive of the present invention is preferably formulated to minimize both acute and long-term risks of leakage that are present when sutures alone are used.

Formulation and storage of sealing media will be described in the titled section page 10.

When applying sealing media in accordance with the present invention, a sufficient amount should be delivered to the tissues or materials so that proper sealing of the joint, perforation, cavity, tear, incision or the like will occur. The media should also be applied in a manner to minimize the risk of embolization or migration. The amount of sealing media to apply in any given case may depend on several factors including the composition of the surfaces to be joined, structure, tissue sensitivity to the media, and the like. Through routine experimentation, however, one of skill in the art should be able to exercise clinical judgment to determine an appropriate quantity of media that will provide effective joint sealing for a particular procedure.

Upon application of the media to the site intended for closure, the two surfaces from which the joint will be formed are brought in contact with each other and the media is allowed to polymerize. Sutures, staples or some other securing means may be used to initially close the joint between the two surfaces, with the application of a sealing medium being a later step to reinforce and thoroughly seal the joint to help prevent leakage or rupture. Alternatively, the two surfaces may be brought together by forceps, clamps or similar devices which are removed once the sealing medium has been applied and allowed to polymerize to set the joint.

Methods of the present invention are preferably directed toward creating a joint by sealing and securing materials, tissues, prostheses, prosthetic devices, grafts, and the like to native tissues in the body of a patient. The need for such a joint formation may arise during surgical procedures.

A suitable formulation of sealing medium comprised of an adhesive compound and a microparticulate component, as described herein, is chosen for use. Characteristics of a medium such as its viscosity, biodegradability and rate thereof, resulting tensile strength upon polymerization, histotoxicity, and polymerization rate, may be taken into account when choosing a medium. Specific characteristics in a medium may be desired to fit needs as dictated by such factors as the nature of the tissues or materials being joined, the location of the joint in the body, and potential stress on the joint.

The method proceeds by bringing together the two surfaces that will form the joint and initially securing them together by conventional techniques involving sutures, staples, or other standard materials and methods known in the art. The joint is then sealed and further secured by applying the chosen sealing medium to the interface of the two surfaces. The method of application may, in part, be determined by factors such as the characteristics of the chosen medium and the geometry, size and placement of the application site. If required, the two surfaces are held together by use of a suitable surgical instrument for the time required for polymerization.

Alternatively, the two surfaces may be brought together by clamps, forceps, hands or other removable means and secured and sealed by means of a chosen sealing medium alone. After polymerization to the point of adhesion, the clamps, forceps or the like are then removed. Thus, the gel or paste of the present invention can be used as the primary securing modality, to replace conventional sutures or staples. The two sides to a percutaneous incision, for example, can be held together and a layer of sealing gel can be placed on the surface to span the incision. After sufficient polymerization, the gel should provide a strong bond while natural healing processes occur.

Another alternate method would be for the sealing medium to be applied to one or both of the surfaces, which are subsequently brought into contact with each other and held for a time long enough to allow for sufficient polymerization resulting in adhesion.

One preferred method of the present invention is the use of sealing media in heart valve replacement. When it is necessary to replace a malfunctioning heart valve within a patient, the most commonly performed procedure requires general anesthesia and a full cardiopulmonary by-pass with complete cessation of cardiopulmonary activity. Descriptions of open-heart procedures for replacing heart valves can be found in Gibbon s Surgery of the Chest., 5th Ed., David C. Sabiston, Jr., M.D., Frank D. Spencer, M.D., 1990, Vol. II, Ch. 52, pp. 1566-1596, and Textbook of Interventional Cardiology, Eric J. Topol, 1990, Chs. 43-44, pp. 831-867.

Once the patient is prepared according to conventional techniques detailed in the references above, the malfunctioning heart valve can be removed and a prosthetic replacement can be implanted. Generally, a tissue cutter is inserted into the patient and advanced to the valve to be severed. The malfunctioning valve is then cut-out and removed from the patient. During this process a continuous flow of clear cardioplegic fluid is maintained to facilitate the observation of the region by the surgeon. After the malfunctioning valve has been severed and removed from the region, the instrument used for cutting is withdrawn and a replacement valve is advanced to the site of implantation.

Replacement valves typically have a Dacron skirt secured to the lower rim of the valve to facilitate securing the replacement valve at or near the site from which the original valve was removed. The replacement valve may also be provided with a temporary or permanent expandable support frame.

The Dacron skirt and support frame is fixed to the appropriate region of the heart by means of a plurality of U-shaped staples. Once the Dacron skirt is secured, the cavities between the stapled tissue and the new valve can be closed one at a time. Closure of a cavity proceeds by delivering sealing medium to the tissue surrounding the cavity and the lower rim of the new valve with or without suturing. A formulation of sealing medium is chosen

to provide a moderate to high past like viscosity, and a relatively low biodegradation rate. A sufficient quantity of sealing medium, preferably 0.25 cc to 1.0 cc, is applied so that the tissue surrounding the cavity, the Dacron skirt, and the lower rim of the new valve is in contact with the medium. Forceps or some other suitable surgical instrument may then used to bring together the tissue between the staples and the lower rim of the new valve and the cavity is held closed until the sealing medium polymerizes. Once the first cavity is closed the surgeon can proceed to the next and so on until the lower rim of the new valve is firmly attached and all cavities are closed. Once the bottom of the valve is firmly attached, the upper extensions of the new valve may be progressively secured using the same approach of stapling followed by using sealing medium to close the cavities detailed above. When the replacement valve is in place, the cardioplegic agents are flushed from the myocardium with saline or blood and the patient is restored according to conventional methods.

Although the present invention has been described in terms of certain preferred embodiments, and certain exemplary applications, it is to be understood that the scope of the invention is not to be limited thereby. Instead, Applicant intends that the scope of the invention be limited solely by reference to the attached claims, and that variations on the formulation and applications disclosed herein which are apparent to those of skill in the art will fall within the scope of Applicant's invention.

Formulation and storage of sealing media

Formulations of sealing media of the present invention preferably comprise a tissue adhesive such as a cyanoacrylate which has been modified to increase its viscosity and, preferably, decrease its polymerization rate. The viscosity of the cyanoacrylate can be increased to a gel or paste form by chemical modification of the cyanoacrylate molecule and/or by the presence of one or more thickening agents. In one embodiment, the sealing medium of the present invention comprises a generally homogeneous mixture of an adhesive compound and a thickener such as a microparticulate component. Any of a variety of other additives can also be added, such as bacteriostatic agents, anti-inflammatory agents, preservatives, stabilizers and the like, as will be understood by those of skill in the art.

Examples of adhesive compounds include cyanoacrylates and fibrin based adhesives. Polymerizable cyanoacrylates that have been cross-linked or co-polymerized with other compounds that may alter elasticity, modify viscosity, aid biodegradation or change some other property of the resulting material may also be used as adhesive compounds in accordance with the present invention. For example, polyacrylic acid having a molecular weight of 200,000 to 600,000 may be cross-linked to a cyanoacrylate to form compounds which may allow the absorbability to be coordinated with the tissue regeneration rate and may feature higher elasticity than cyanoacrylates alone. Absorbability is unnecessary for topical applications, in which the adhesive film will simply fall off in a few days.

Microparticulate components in accordance with the present invention may include silica, and tiny beads or pieces of polymeric materials such as polymethylmethacrylate (PMMA). Preferably, formulations of sealing media comprise cyanoacrylate as the adhesive compound and silica as the microparticulate component.

Among the reasons why cyanoacrylates are preferred are that they have several particular advantages as an adhesive compound. First, they harden almost instantaneously on contact with surfaces having moisture thereon. This includes most tissues and surfaces in and on the body of an animal, such as a human. Second, experiments by the inventor indicate that cyanoacrylate sealed vascular punctures can withstand several times the maximum potential systolic pressure, and hence, would not be expected to fail when used to seal a joint such as at the annulus of a heart valve or to seal most surface wounds. Also, cyanoacrylates are naturally thrombogenic. This is an advantage in certain applications as it promotes the first step in healing.

Preferred adhesive compounds to be used in the media of the present invention comprise compounds within the cyanoacrylate family. Such compounds include methyl cyanoacrylate, ethyl cyanoacrylate, n-propyl cyanoacrylate, isopropyl cyanoacrylate, n-butyl cyanoacrylate, isobutyl cyanoacrylate, n-amyl cyanoacrylate, isoamyl cyanoacrylate, 3-acetoxypropyl cyanoacrylate, 2-methoxypropyl cyanoacrylate, 3-chloropropyl cyanoacrylate, benzyl cyanoacrylate, phenyl cyanoacrylate, alkenyl cyanoacrylate, butyl-2-cyanoacrylate, alkoxyalkyl 2-cyanoacrylates, fluorinated 2-cyanoacrylates, and carbalkoxyalkyl cyanoacrylates, depending upon acceptable toxicity and other properties for a given application. More preferably the adhesive compound comprises ethyl cyanoacrylate or butyl-2-cyanoacrylate. These latter two compounds, are available commercially from Loctite Corporation (Hartford, Conn.) or Pacer Technology (Rancho Cucamonga, Calif). Other members of the cyanoacrylate family may be commercially available or may be synthesized according to published procedures or analogous methods as is within the abilities of one skilled in the art.

The above-listed members of the cyanoacrylate family as well as other members of the cyanoacrylate family and other adhesive compounds that fall within the scope of this invention and are not listed above, may differ in their properties when used in a surgical sealing medium. The efficacy, histotoxicity, and other medically relevant properties of above-listed and other members of the cyanoacrylate family can be readily determined by routine experimentation by one of ordinary skill in the art. Such experimentation will enable one skilled in the art to choose a suitable cyanoacrylate or other adhesive compound for use in the media of the present invention.

Depending upon the nature of the placement and composition of the two surfaces to be joined, the degree of biodegradability or bioabsorbability desired in the sealing medium employed may vary. Where one of the surfaces to be joined is a nontissue material such as Dacron or stainless steel, it may be preferable to use a sealant medium that is substantially nonbiodegradable. For wounds or incisions on the surface of the skin, it may be preferable to use a sealant medium that is substantially nonbiodegradable. Alternatively, where both surfaces are living tissue, such as two sides to an incision or an autologous tissue graft, it may be preferable to use a sealing medium that will biodegrade over a period of days or weeks, diminishing as the natural healing mechanisms take hold.

There is a wide variation in the rates and facility of *in vivo* biodegradation of polymers made from monomers which may be used as adhesive compounds in the present invention. There is also a wide variation in such rates among the members of the cyanoacrylate family, the preferred adhesive compounds of the present invention. Generally, polymers of cyanoacrylates which have substituents that are small and/or contain one or more

oxygen-containing functional groups (e.g. ether, ester, carbonyl) appear to have increased biodegradability rates. Cyanoacrylates having long chain alkyl groups lacking in oxygen-containing functional groups as substituents may tend to form polymers which biodegrade more slowly. There are also indications in the literature that the biodegradation rate of cyanoacrylate polymers is affected by the polymer molecular weight and crystallinity of the polymer.

There are several studies of biodegradation rates of polymers formed by various members of the cyanoacrylate family in the scientific and medical literature. It is within the abilities of one of skill in the art to use such information in the literature along with routine experimentation in order to choose a member of the cyanoacrylate family with suitable biodegradation characteristics for use in accordance with the present invention.

Microparticulate silica is commercially available in a variety of different particle sizes. That which is preferred is generally less than about 10 microns in average diameter, more preferably 0.01 to 1 micron, most preferably 0.01 to 0.1 microns for certain applications. Variations in the quantity and particle size of silica used will result in media which differ in properties. Optimization for particular formulations can be accomplished through routine experimentation.

Among the properties that change with the quantity of silica or other microparticulate modifier used are viscosity and polymerization rate. Increasing the percentage (weight to volume) of silica in the medium will increase the viscosity of the medium in a generally linear manner. Increased viscosity provides for easier application of the media on tissues, as viscous media stay where they are placed and thus decrease the incidence of running or dripping onto other surfaces or tissues, or leaking in between sides of a laceration to be closed. As the viscosity of a given medium is increased, the polymerization rate of that medium concomitantly decreases. Decreased polymerization rates allow more time for a practitioner to place and adjust the surfaces that are to be sealed. Where the polymerization time is short, there can be little if any margin for error before the surfaces are sealed. The longer polymerization time has an additional benefit. Since the polymerization process is exothermic, decreasing the polymerization rate decreases the rate that heat is released by the medium, resulting in a lower temperature in the medium and surrounding tissues during polymerization.

An additional property that may change with added silica is the toxicity. An experiment to determine cytotoxicity was performed using standard MEM (minimum essential medium) elution techniques. Two polymers, one formed by a commercial preparation of liquid ethyl cyanoacrylate (Aron Alpha from Toagosei, Ltd.) and the other from a medium of the present invention, a gel comprised of 3% by weight fumed silica (Cabot Corporation, Cab-O-Sil Division, Tuscola, IL) in ethyl cyanoacrylate were extracted for 24 hours in MEM. Mouse cells were exposed to the extracts and were examined at 48 and 72 hours for evidence of cytotoxic effects. There was extensive crenation (shrinking or scarring of cells) and 90% lysis observed in cells exposed to the extract of the commercial ethyl cyanoacrylate adhesive. This extract was thus adjudged to be toxic. In contrast, there was no crenation and 0% lysis in cells exposed to an extract of the medium comprising silica, which was thus adjudged to be non-toxic.

There is also some evidence that joints formed between two surfaces by media of the present invention have a greater flexibility and tensile strength than joints formed by adhesive compounds alone, without a microparticulate modifier.

In some embodiments, formulations of sealing media may additionally comprise one or more optional additives, such as polymers, viscosity modifiers, colorants, anti-diffusion agents, salts, antibiotics, anti-microbials, stabilizers, dessicants, catalysts, or agents that slow polymerization.

Generally, formulations of sealant media for the present invention comprise generally homogeneous mixtures of at least one adhesive compound with preferably 1% to 5% (by weight) microparticulate component. Preferred formulations of sealant media for the present invention comprise generally homogeneous mixtures of at least one cyanoacrylate with preferably 0.25% to 8% (weight) silica, more preferably 1% to 5% (weight) silica, most preferably 1% to 3% (weight) silica.

Proper storage of sealing media is an important consideration. Many cyanoacrylates will polymerize and harden relatively rapidly when stored below a critical volume. Hence, if a cyanoacrylate is used as the adhesive compound, it will be preferable for the vessel or reservoir in which the sealing medium is stored to contain more medium than is necessary to seal a typical site. Preferably, the storage vessel or reservoir should contain a minimum of 1 to 5 grams, more preferably 3 to 4 grams of medium to maintain the cyanoacrylate component of the medium in a generally unpolymerized state in the storage vessel or reservoir prior to use. The total volume of medium, the desiccation measures, and the sealing structures on the storage vessel or reservoir may be optimized to produce enhanced shelf life by one of skill in the art.

Any of a variety of containers or devices can be used to deliver media to a site intended for sealing. For example, syringes, eyedroppers, compressible bottles or tubes, tongue depressors, spatulas, or others can be used to deliver media to the site intended for sealing. Media in paste form can be scooped manually from a jar or other container by fingers and manually packed around the base of the heart valve or other joint to be sealed or on the wound to effect closure. Additionally, devices designed to deliver sealing media may be used, such as those of the type disclosed in U.S. Patent No. 5,529,577. The choice may, in part, be determined by the viscosity of the medium employed, which is dependent upon factors such as the viscosity of the adhesive compound, the particle size of the microparticulate component, and the relative amounts of adhesive compound and microparticulate component. The choice of delivery means may also depend on other factors such as the nature of the tissues or materials to be joined and the physical structure of the joint to be sealed. The choice may also depend on the nature, physical structure or location on the body of the wound to be closed and sealed. It should be understood that this list and the devices mentioned above are meant to be merely illustrative, and that one of skill in the art may develop alternate means to deliver sealing media to the sites wherein they are used.

Sealing media for wound closure:

In accordance with the present invention, a sealing medium is used to join adjacent surfaces of skin to effect closure of a wound or incision. The gel or paste sealing media of the present invention are typically used as

the primary closure modality, to replace conventional sutures or staples. The two sides to a percutaneous incision, for example, can be held together and a layer of sealing gel can be placed on the surface to span the incision. After sufficient polymerization, the gel will provide a strong bond while natural healing processes occur. It is preferred that the sealing media of the present invention are used as the primary method of wound closure, but they may be used in conjunction with other wound closure or tissue fastening systems, such as staples and sutures, or in combination with a support structure such as cloth or gauze.

Although specific closure means and support structures are identified and discussed in this specification, such use of the terms should not be construed as limiting the definitions of these terms. It is the applicant's intention that these terms be given their broad ordinary meanings.

The present invention may be used to effect wound or percutaneous incision closure in a manner that is quick, simple, and effective. The materials and methods of the present invention require little training for their use and may be used by medical personnel to replace conventional methods of closing wounds. Additionally, they may be used by non-medical persons for use in combination with or as a replacement for conventional home remedies, such as adhesive bandages.

Formulations and storage of sealing media of the present invention are descibed in the previous section, page 10.

The wound closure media of the present invention are preferably stored and applied using a container-applicator. A container-applicator has two basic parts: (1) a storage area or reservoir which holds the media and protects it from air, water and contaminants; and (2) the applicator which comprises a specially shaped tip designed to aid in application of media.

The reservoir is preferably both air-tight and water-tight, and keeps the media within free from contaminants. The reservoir may contain a desiccant material to keep the media free of water, which would cause polymerization of the preferred cyanoacrylate-based media. Reservoirs may be of any shape, although shapes which provide for a smooth internal flow of media, such as cylindrical or pyramidal shapes, are preferred. The size of the reservoir may vary within a wide range, but is preferably slightly larger than the volume of media which will be placed inside the reservoir to minimize the amount of gas within the reservoir. The reservoir may be made from any of a variety of medical grade materials, such as plastics, that is suitable for the storage of cyanoacrylates as is known in the art. The reservoir may be either rigid, collapsible, or compressible. Use of a compressible or collapsible reservoir allows the user to have greater control over the rate at which media is expressed, as exertion of pressure on a compressible or collapsible reservoir would place a force on the on the media causing it to flow at a faster rate than it would in the absence of such pressure. The compressible or collapsible reservoir design is especially preferred for highly viscous or gel-like media for which the force of gravity may not be strong enough to cause a flow of media through an applicator sufficient to close a wound. Collapsible reservoirs which retain their collapsed shape have the additional advantage of reducing the amount of air which enters the reservoir following

use. This advantage of collapsible containers is of greater importance in multiple-use (reuseable) devices, wherein media is preferably kept relatively free of potential contaminants between uses.

Applicator tips can be of any of a number of shapes, sizes, and configurations. They are preferably fairly rigid and may be made out of any material which is compatible with the media formulation, preferably plastic. The choice of a proper applicator tip for a given application will depend on factors such as the viscosity of the media, the desired application rate of the media, the nature of the wound, the placement of the wound on the body, and the physical structure of the wound.

The container-applicators of the present invention may be either single-use or multiple-use devices. For most applications, single-use container-applicator devices are preferred. This preference arises because the risk of cross-contamination between wounds or patients is practically eliminated when a new device is used for each closure. As an alternative to the single-use embodiment, a container or reservoir containing enough media for multiple closures may be configured to accommodate replaceable tips. In such an embodiment, at the place whereon the replaceable tips connect with the reservoir, the reservoir would preferably have a means such as a valve, septum or sealing gasket which allows the reservoir to be sealed in the absence of an applicator tip. Placing an applicator tip on the reservoir would cause the valve to open, allowing media to flow out from the reservoir. In this manner, one reservoir containing enough media to close several wounds could be used over a period of hours, days or weeks. This embodiment would also allow the user to use one reservoir with applicator tips of varying shapes and sizes chosen to best accommodate the needs of different wounds.

Two specific embodiments of container-applicators are depicted in the drawings and detailed below. These embodiments are presented as illustration only, as it is the inventor's intention that the invention be limited only by the scope of the attached claims, and not exclusively to the embodiments disclosed with particularity herein.

One preferred embodiment of container-applicator is the rollerball container-applicator 1 depicted in Figure 1. The reservoir 2 may be either rigid, compressible, or collapsible and may be made out of any material suitable for the storage of cyanoacrylates, as is known in the art. The applicator tip portion of the container-applicator comprises a ball 3 and a cuff 4. The ball 3 is held loosely within the cuff 4 so that the ball 3 is free to rotate in any direction, but not so loosely as to allow the ball 3 to be removed or fall out when the container-applicator 1 is inverted. The size of the gap 5 formed between the ball 3 and the cuff 4 can be varied to accommodate a wide range of viscosities of media and desired flow rates. For low viscosity media, a relatively small gap 5 would be preferred to allow the media to flow out around the ball at a reasonable rate during application, whereas for high viscosity gel-like media a larger gap 5 would be required to allow a reasonable flow of media around the ball 3. Similarly, the gap 5 can be varied to achieve a desired application rate for media of a particular viscosity. For media of a given viscosity, a large gap 5 would provide a higher flow rate for the media than a smaller gap 5. Furthermore, use of a compressible or collapsible reservoir 2 allows for additional control over the rate at which media is expressed, as exertion of pressure on the compressible reservoir increases the pressure on the media

causing it to flow through gap 5 at a rate faster than that for the same media in the absence of exerted pressure, regardless of viscosity.

A second embodiment of container-applicator is that depicted in Figure 3. This embodiment comprises a container such as pyramidal reservoir 11 and an applicator tip 12. The container-applicator 10 may further comprise a one-time removable or breakable sealing tip or cap as described below. In the illustrated embodiment, the media flows from the reservoir 11 through a tubular extension 12 and out to the application site through an opening 13 in the flared distal end of the applicator tip 14. In one preferred embodiment, the length of the extended portion 12 of the applicator tip 14 is preferably 0.1 to 10 cm long, more preferably 0.5 to 2 cm, but can be readily optimized in view of an intended use for the applicator 10. The largest cross-section of the flared end can also come in a wide range of sizes, preferably from 0.5 to 5 cm, generally less than 2 cm, but it is most preferably chosen to be a little larger than the width of the wound to be closed. The configuration of the opening 13 may be a narrow elliptical or rectangular slot or other configuration suited for the end use. The reservoir 11 is preferably compressible or collapsible to allow for greater control in the rate at which the media is expressed from the opening 13.

In one embodiment, the distal opening 13 of the applicator tip 14 has a shape like that shown in Figure 4. During application, the flattened side is placed towards the skin to maximize the area of applicator-skin contact. This semi-elliptical or other concave shape of the opposing side of opening 13 results in application of a rounded strip of sealing medium as the tip 14 is drawn across the surface of the skin.

The applicator tip of the container-applicator may further comprise a removable or breakable sealing tip. One embodiment of a breakable sealing tip, which may be used for a single-use device, is shown in Figure 5. The applicator cap 15 forms a solid covering for the opening of the applicator tip (14 in Figure 5). The applicator cap 15 is preferably of the same material as the applicator tip 14, the two parts meeting at a breakline 16. In one embodiment in which the tip 14 and cap 15 are integrally formed, the breakline 16 is characterized by scoring or other means which weakens the junction and allows the two parts to be easily separated by grasping the two parts (12 and 15) in either hand and bending or tearing the pieces apart to expose the opening 13 in the applicator tip 12 through which the media is expressed. The cap 15 can alternatively be press fit or threadably engaged within or over the distal tip 14 and retained by friction as will be apparent to those of skill in the art.

Alternatively, a single-use device may comprise a reservoir wherein the opening through which the media flows is covered with a peelable or puncturable plastic film or metal foil. In one such embodiment, the foil or film is peeled back or pierced prior to positioning the applicator and sealing the wound. In another embodiment, the applicator portion has a proximally extending point or projection which pierces the foil or film as it is threaded onto or otherwise secured to the reservoir.

One embodiment of container-applicator is a single-use, sterile wound closure device. Preferably such a device has a pierceable or removable tip seal. The container portion of the preferred single-use wound closure device is sized to hold preferably from 2 to 10 grams, more preferably 2 to 5 grams of wound closure media,

depending upon the intended use. The container may be of any of a variety of standard container shapes, and is preferably compressible or collapsible so that the user may control the rate at which the media contained therein is expressed by varying the pressure exerted on the walls of the container.

The single-use sterile wound closure device is prepared by first taking a clean container that will serve as the reservoir and filling it with wound closure media comprising an adhesive component and a microparticulate component. The reservoir is then sealed. Sealing the reservoir is preferably done by affixing an applicator tip with a removable seal to the reservoir, or by securing a pierceable septum to the container. The container-applicator, with the wound closure media sealed inside, is then sterilized by methods known to those skilled in the art which may be used on the materials from which the container-applicator is made and which will also not react with the adhesive component of the media.

In the alternative, the pieces which comprise the container-applicator can be pre-sterilized, and the device filled and sealed in a sterile or ultra clean environment. This is potentially a viable method, as the preferred formulation of wound closure media, that comprising cyanoacrylate and silica, is generally not supportive of the growth of microorganisms.

The use of reusable coverings for applicators or applicator openings, such as caps, plugs, valves, or the like are also contemplated. Use of this type of covering would allow a container or container-applicator to be used several times before it is discarded.

The containers, applicators, and container-applicators disclosed above may be used alone, in combination with a support structure, such as a piece of cloth, gauze or mesh, or in addition to some other conventional securing means such as sutures or staples. Support structures can provide an extra measure of strength and protection for the wound, while use of a sealing medium with sutures or staples can reinforce and thoroughly seal the joint to help prevent rupture, protect the joint from abrasion, or keep it free of debris. Similarly, for a deep or penetrating wound or surgical incision, the innermost tissues may be joined by dissolvable sutures while the exterior surface is joined using media according to the present invention.

Closure of a wound may also be effected by the use of a device comprising a support structure impregnated with media. In such a device, the support structure, comprising cloth or gauze, has a sufficient quantity of media imbedded therein to allow for closure and sealing of a wound. Preferably, each device is individually sealed within air-and-water-tight packaging such as a plastic or foil pouch until use. Although the application and use of such a device would be very similar to a conventional adhesive bandage, it has several advantages. The media impregnated support structure will adhere to the wound for a much longer time than a conventional adhesive bandage and provide a better barrier to water, dirt, and abrasion. The media impregnated support structure would be especially suitable for use on children, as it would keep the wound cleaner and prevent the child from disturbing the wound and hampering the healing process.

When applying media of the present invention, the surfaces of the wound, laceration, percutaneous incision, or the like intended for closure are brought in contact with each other by use of the fingers, forceps, or a

similar device. A sufficient amount of medium is delivered to the surface so that proper sealing and closure retention will occur. When sealing the joint formed by the sides of the wound, laceration, or percutaneous incision, the medium is applied to the exterior surface of the wound and allowed to polymerize so that it forms a film over the entire wound. Preferably, media are applied in a manner to minimize the amount of medium which seeps between the edges of a wound. The amount of sealing medium to apply in any given case, and thus the area and thickness of the resulting film, may depend on several factors including placement of the wound on the body, depth of the wound, tissue sensitivity to the media, and the like. Media may be applied alone or in combination with a support structure or a more conventional securing means such as sutures. Through routine experimentation, however, one of skill in the art will be able to exercise clinical judgment to determine an appropriate quantity of medium to provide effective closure for a particular procedure.

Methods of the present invention are preferably directed toward closing and sealing a wound by sealing and securing together adjacent tissues, such as opposing pieces of skin, in a patient. The need for closure of such a wound may arise during surgical procedures, as a result of percutaneous incision. The need may also arise as a result of traumatic injury resulting in a laceration or other wound which breaks the skin.

Generally, a method of closing a wound, laceration, percutaneous incision, or the like proceeds by first assessing what type of closure or combination of closures is proper for a wound given factors such as the size, depth, and location of the wound as well as an assessment of the overall needs and requirements of the patient. Such assessments are routinely done by those skilled in the medical arts. In a non-clinical setting, the assessment step will likely be much more cursory.

Next, a suitable formulation of sealing medium, an applicator, and a method of application are chosen. These three choices are somewhat interconnected, as the choice of a particular applicator constrains the method of application, and a particular formulation of media may constrain the type of applicator or method of application which can be used, and vice-versa.

The choice of a suitable formulation of wound closure medium comprising an adhesive compound and a microparticulate component, as disclosed herein, may depend upon characteristics of a medium such as its viscosity, biodegradability and rate thereof, resulting tensile strength upon polymerization, flexibility when polymerized, histotoxicity, and polymerization rate. Specific characteristics may be desired to fit clinical needs as dictated by factors such as the size of the wound, the amount and rate of bleeding from the wound, the location of the wound on the body, and potential stress on the sealed wound.

The choice of applicator and method of application may, in part, be determined by factors such as the composition, viscosity, and polymerization time of the medium, and the geometry, size and placement of the application site. Such a choice may also be constrained by the tools and devices available to the user. Examples of preferred applicators are disclosed above and examples of preferred methods of application are described below.

Next, the wound may need to be prepared before closure. Activities involved in wound preparation are highly situational, but are routinely done by those skilled in medicine, nursing, and related arts. Wound preparation

may involve tasks such as removal of debris, dirt, oil, or excess tissue from the wound, application of pressure or similar measures to bring about the cessation of bleeding, cleansing the wound, application of an antimicrobial preparation, use of a conventional closure means such as sutures, and other such tasks. In a non-clinical setting, the patient or use may also perform some of these same tasks.

If the surfaces of the wound naturally pull apart, the two surfaces should be brought into contact with each other and properly aligned to achieve minimal scarring by use of the fingers, support structure, forceps or other suitable medical instrument. In such a case, the two surfaces are preferably held together as the medium is applied and afterwards until sufficient polymerization has taken place to allow the closure to be self-supporting. Alternatively, the two surfaces may be brought together by sutures, staples, tape or other securing means and then further sealed by application of a chosen medium. In wounds for which the skin is not separated, this step may be skipped.

The chosen medium is then applied using the applicator and method chosen in an earlier step. The entirety of media application is preferably done within a limited period of time, as the strength of the closure formed by two or more successive applications of media (wherein one application has been allowed to polymerize before the next application) may not be as strong as the closure formed by one application allowed to polymerize to form a single layer on the skin surface. Media is applied in a quantity sufficient to effect wound closure and sealing. More may be applied, if desired, to increase the strength of the closure or likewise, a support structure may be applied. Determination of quantity of media applied can be determined by routine experimentation and exercise of clinical judgment. Specific methods of application involving the use of container-applicators are discussed in the paragraphs which follow.

One specific method of application is that involving the use of the rollerball container-applicator pictured in Figure 1. To use this container-applicator, first any sealing means is removed or broken. Then, as depicted in Figure 2, the container is tipped so that the rollerball is pointing in a generally downward direction and the bottom of the reservoir portion is pointing in a generally upward direction. Such orientation of the container-applicator facilitates the flow of media towards the rollerball applicator portion through which it may then be applied to the wound. Preferably the media is applied by moving the container-applicator back and forth over the surface of the wound and surrounding skin areas while keeping the rollerball in contact with the wound at all times. Although a back and forth movement is preferred, any movement of the applicator which serves to deliver the media to the intended site without disturbing the wound itself is contemplated.

If the reservoir portion of the container-applicator is compressible or collapsible, the rolling of the applicator over the surface of the skin can be accompanied by squeezing or otherwise compressing the walls of the reservoir. With such a collapsible or compressible reservoir, the rate of flow of media and therefore the amount of media delivered, is proportional to the amount of pressure applied to the walls of the reservoir. The quantity and rate of media delivery can thus be controlled by the user.

Another specific method of application is that using a container-applicator of the type depicted in Figure 3. To apply media, first any sealing means such as a foil seal, peelaway thin film or breakable tip is punctured or removed to allow for flow of media. The applicator tip is preferably placed on or slightly above the surface of the wound to be sealed. If a hemi-elliptical tip is used, such as that pictured in Figure 4, the flattened side is preferably placed closest to the skin. The media is then allowed to flow through the applicator and onto the surface of the skin. Preferably, the reservoir portion comprises collapsible or compressible walls such that the user may exert pressure on the walls to facilitate the delivery of media to the skin, and thus control the rate at which the media is expressed from the applicator tip. The tip is moved over the surface of the skin, following the contours of the wound, resulting in the deposition of a strip of media on the skin covering the wound. Additional strips may be laid down in a similar manner to thicken or expand the area of media coverage.

In accordance with another embodiment of the present invention, the reservoir is provided as a separate component from the applicator tip. In this embodiment, the reservoir is provided with a pierceable seal or septum, such that a unit volume of media can be sealed within the reservoir. Pierceable septums or seals comprising silicone, other polymeric materials known in the medical industry, as well as metal foils or thin polymeric films may be utilized, as will be apparent to those of skill in the art in view of the nature of the complimentary piercing structure on the applicator tip.

The detachable applicator tip comprises an applicator surface on a distal side thereof, and a cannula, needle or other piercing structure projecting proximally from a proximal side thereof. A retention structure is preferably also provided, for securing the applicator tip to the reservoir. In one embodiment, the retention structure is an axially extending annular flange having a thread on the radially inwardly or outwardly facing surface thereof, for threadably engaging the top of the reservoir. Any of a variety of other retention structures can be utilized, as will be apparent in view of the disclosure herein.

Prior to use at the clinical site, the applicator tip is secured to the reservoir such that the proximally extending piercing member on the proximal side of the applicator tip pierces the septum or other seal on the reservoir, thereby placing the contents of the reservoir in fluid communication with the distal applicator surface. This embodiment is particularly suited for a one-time use disposable device. The applicator surface can be of any of a variety of structures disclosed elsewhere herein, such as a rollerball, or a specially configured opening such as a slot, for expressing a thin layer of sealing media over the surface of the tissue on either side of a wound.

Any of the foregoing methods may be combined with the application of a support structure such as gauze. A layer of media is first applied to the wound, onto which gauze or other support structure is affixed, the media acting to secure the gauze in place. More media may then be applied over the gauze to further secure it and strengthen the closure. In the alternative, gauze may be first placed over the wound and then covered and secured to the wound by subsequent application(s) of media as described above. In either case, alternate layers of media and gauze may be applied to form a flexible, reinforced structure which effects closure of the wound and sealing.

As an alternative to the method discussed above, a prepackaged media-impregnated support structure may be applied to the wound to achieve closure. Such a device, as described above, is preferably packaged in a sealed pouch and comprises a support structure, such as a section of cloth, that is saturated with a quantity of media sufficient to allow for attachment of the support structure and effect closure of a wound or section of a wound of a size corresponding to the size of the support structure. Closure of a wound using such a device is somewhat comparable to using a common adhesive bandage and is particularly well-suited for non-clinical use. First, the pouch containing the device is opened and the device removed therefrom. The device is then placed over the surface of the wound and then pressed into place to ensure good contact between the device and the skin. If additional coverage is required or desired, additional devices may be applied. When more than one device is used, they are preferably applied within a short time of each other so that they polymerize at nearly the same time.

WHAT IS CLAIMED IS:

1. A medical grade sealing media for sealing a surface to a tissue of a mammal, said sealing media comprising an adhesive with a microparticulate material dispersed therein.

2. The medical grade sealing media of Claim 1, wherein said adhesive is selected from the group consisting of cyanoacrylates and cyanoacrylate derivatives.

3. The medical grade sealing media of Claim 1, wherein said microparticulate is selected from the group consisting of silica, tiny beads, and pieces of polymeric material.

4. The medical grade sealing media of Claim 2, wherein said microparticulate is silica.

5. The medical grade sealing media of Claim 1, wherein said microparticulate material has an average diameter between 0.01 and 10μ.

6. The medical grade sealing media of Claim 1, wherein said microparticulate material has an average diameter between 0.01 and 1μ.

7. The medical grade sealing media of Claim 1, wherein said microparticulate material has an average diameter between 0.01 and 0.1μ.

8. The medical grade sealing media of Claim 1, wherein the microparticulate component is between 0.25 and 8% by weight of the sealing media.

9. The medical grade sealing media of Claim 1, wherein the microparticulate component is between 1 and 5% by weight of the sealing media.

10. The medical grade sealing media of Claim 1, wherein the microparticulate component is between 1 and 3% by weight of the sealing media.

11. The medical grade sealing media of Claim 1, wherein said surface is native tissue from said mammal.

12. The medical grade sealing media of Claim 1, wherein said surface is a surface which is not tissue.

13. The medical grade sealing media of Claim 1, wherein both said surface and said tissue are skin.

14. The medical grade sealing media of Claim 11, wherein said native tissue is a harvested vessel.

15. The medical grade sealing media of Claim 1, wherein said tissue is a non-native tisse selected from the group consisting of donor organs, donor tissue, donor heart valves, and donor grafts.

16. The medical grade sealing media of Claim 12, wherein said surface is selected from the group consisting of stainless steel, gold, platinum, polyethylenes, nylons, polypropylenes, polytetrafluoroethylene, other polyfluoro compounds, polyesters, and other polymeric materials.

17. The medical grade sealing media of Claim 1 further comprising one or more additives selected from the group consisting of polymers, viscosity modifiers, colorants, anti-diffusion agents, salts, antibiotics, antimicrobials, stabilizers, perfumes desiccants, catalysts, and agents that slow polymerization.

18. Use of the sealing media according to any of the foregoing claims in the preparation of a medicament for sealing a surface to a tissue of a mammal.

19. A wound closure device, comprising:

a reservoir containing wound closure media, said wound closure media comprising the medical grade sealing media of Claim 1; and an applicator tip.

20. The wound closure device of Claim 19, wherein said reservoir is collapsible or compressible.

21. The wound closure device of Claim 19, wherein said applicator tip comprises a rollerball.

22. The wound closure device of Claim 19, further comprising an elongated hollow tube having a proximal end and a distal end, wherein said proximal end is attached to said reservoir and said distal end comprises the tip.

23. The wound closure device of Claim 19, further comprising a removable seal on said applicator tip.

24. The wound closure device of Claim 19, wherein said applicator tip is resealable.

25. The wound closure device of Claim 19, wherein said device is sterilized.

26. The wound closure device of Claim 19, wherein said device is disposable.

27. A wound closure dressing, comprising:

a flexible support structure impregnated with wound closure media, said wound closure media comprising the medical grade sealing media of Claim 1.

28. The wound closure dressing of Claim 27, further comprising a sealed pouch surrounding and containing said wound closure dressing therein.

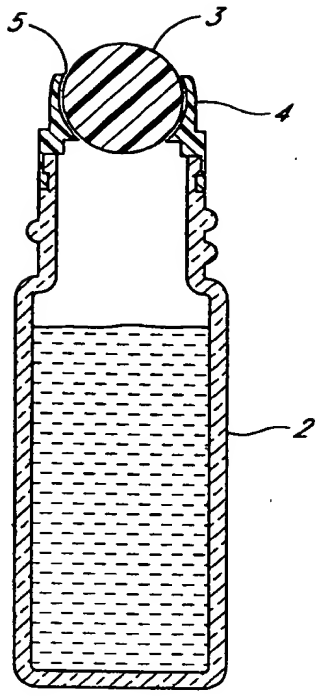


FIG. 1

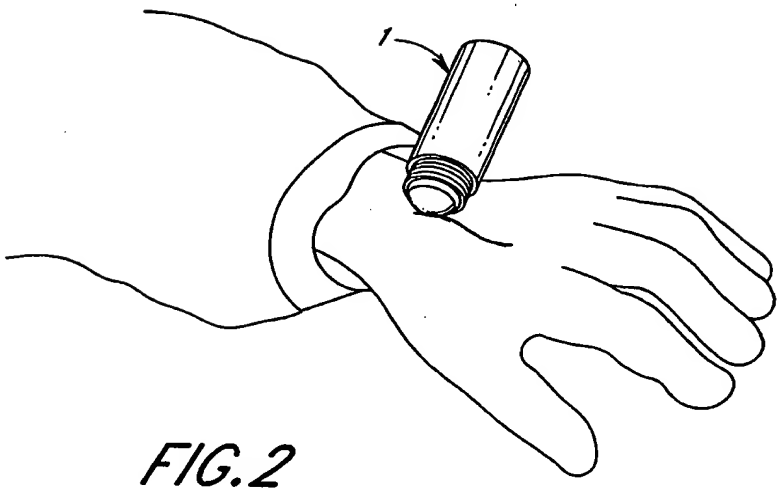


FIG. 2

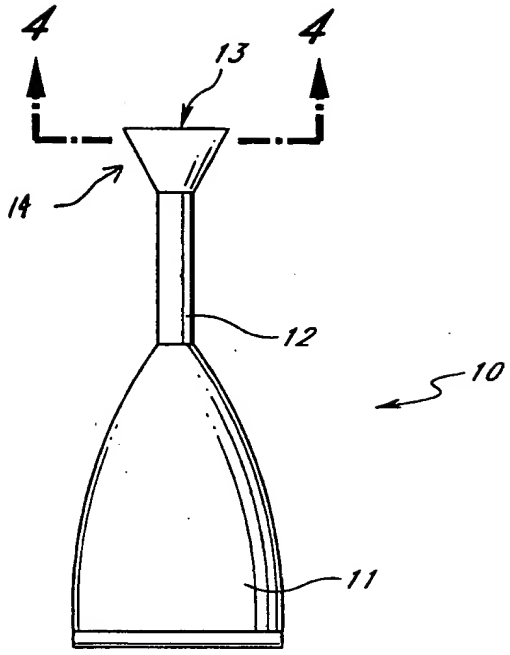


FIG. 3

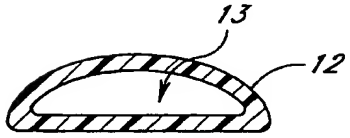


FIG. 4

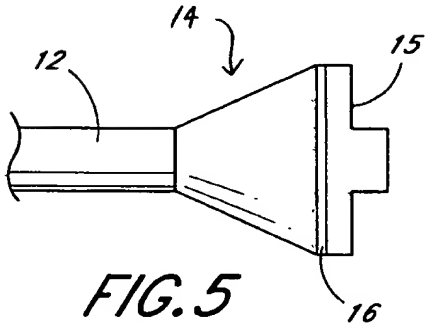


FIG. 5

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/26825

A. CLASSIFICATION OF SUBJECT MATTER
IPC(6) :A61B 19/00
US CL :128/898
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 128/898

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
APS
Search Terms: cyanoacrylate, silica, particulate, adhesive

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,350,798 A (LINDEN et al.) 27 September 1994, entire disclosure.	1-28
Y	US 5,248,708 A (UEMURA et al.) 28 September 1993, entire disclosure.	1-28
Y	US 5,529,577 A (HAMMERSLAG) 25 January 1996, entire disclosure.	19-28
Y	US 5,222,939 A (TIEFENBRUN et al.) 29 June 1993, entire disclosure.	19-28

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search
01 MARCH 1999

Date of mailing of the international search report
31 MAR 1999

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231
Facsimile No. (703) 305-3230

Authorized officer
DINH XUAN NGUYEN
Telephone No. (703) 305-3522

Form PCT/ISA/210 (second sheet)(July 1992) ★